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EXAMINER

TUNGATURTHI, PARITHOSH K

ART UNIT	PAPER NUMBER
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1643

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12/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/519,580

Applicant(s)

KASHMIRI ET AL.

Examiner

Parithosh K. Tungaturthi

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6,8,10-12,16,20-28,32-35,44,45,47,48,52,56 and 67 is/are pending in the application.
- 4a) Of the above claim(s) 21,22,32-35,44,45,47 and 48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6,8,10-12,16,20,23-28,52,56 and 67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/27/2004;05/05/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-4, 6, 8, 10-12, 16, 20, 23-28, 52, 56 and 67, in the reply of 09/24/2007 is acknowledged.
2. Claims 21, 22, 32-35, 44-45, 47 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.
3. Claims 1-4, 6, 8, 10-12, 16, 20, 23-28, 52, 56 and 67 are under examination.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claims 56 is vague and indefinite in the recitation of "HuCC49V10" as the sole means of identifying the antibody. The use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. This rejection can be obviated by amending the claims to specifically and uniquely identify, for example, by SEQ ID NO.
6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 20, 23, 56 and 67 is rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if the CC49 antibody, HuCC49V10 antibody and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183 are known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above nucleic acid sequences, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed nucleic acid sequence encoding the humanized CC49 antibody; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

It is noted that the specification states the humanized CC49 antibody includes a nucleic acid sequence encoding the antibody that is deposited as ATCC Accession number PTA-4182 or ATCC accession number PTA-4183 (page 2, in particular).

However, the specification lacks complete deposit information for the deposit of the CC49 antibody, HuCC49V10 antibody and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183. It is not clear that such nucleic

acid sequence is known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Applicant's failure to refer to the deposit information pertaining to the CC49 antibody, HuCC49V10 antibody and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183 in the specification is noted and it is required that the required deposit be made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit of the CC49 antibody, HuCC49V10 antibody and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183 is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of the CC49 antibody, HuCC49V10 antibody and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183 has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of the CC49 antibody, HuCC49V10 antibody and the nucleic acid sequence having the ATCC accession numbers PTA-4182 and PTA-4183 is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits

comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

- (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;
- (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;
- (c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and
- (d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90

(CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

8. Claims 1-4, 6, 8, 10-12, 16, 23-28, 52, 56 and 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a humanized CC49 antibody, comprising: a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, wherein a L-CDR3 of the humanized CC49 antibody or of the antigen binding fragment of the humanized CC49 antibody comprises a non-conservative amino acid substitution at position 91, wherein the tyrosine at position 91 is substituted with proline (HuCC49V10-14), and wherein the humanized CC49 antibody has a high binding affinity for TAG-72, compared to a parent CC49 antibody, wherein all the CDRs are from a parent human CC49 antibody, wherein the parent antibody is HuCC49V10 AND a humanized CC49 antibody, comprising: all four variable light chain framework regions and all four variable heavy chain framework regions of a human antibody; a light chain complementarity determining region (L-CDR)1, a L-CDR2, a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, wherein at least one complementarity determining region (CDR) is a human antibody CDR and remaining CDRs are murine CC49 antibody CDRs; a non-conservative substitution of at position 91 in the L-CDR3 of the antibody, wherein the tyrosine at position 91 is substituted with proline; and a second substitution at position 27b of L-CDR1, wherein the valine at position 27b is substituted

with leucine (HuCC49V10-15), wherein the humanized CC49 antibody has a high binding affinity for TAG-72, compared to a parent CC49 antibody, wherein the parent antibody is HuCC49V10, **does not reasonably provide enablement for** a humanized CC49 antibody, comprising: a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, wherein a L-CDR3 of the humanized CC49 antibody or of any functional fragment of the humanized CC49 antibody comprises a non-conservative amino acid substitution at any position OR at any tyrosine residue of L-CDR3 OR substituting the tyrosine residue at position 91 with any amino acid, and wherein the humanized CC49 antibody has a high binding affinity for TAG-72, compared to a parent CC49 antibody OR a humanized CC49 antibody, comprising: a variable light framework region and a variable heavy framework region of a human antibody; a light chain complementarity determining region (L-CDR)1, a L-CDR2, a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, wherein at least one complementarity determining region (CDR) is a human antibody CDR and remaining CDRs are murine CC49 antibody CDRs; a non-conservative substitution of any residue is in the L-CDR3 of the antibody; and a substitution of any residue in any L-CDR or H-CDR of the antibody; wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988).

Wands states on page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention is engineered antibodies where the relative level of skill of those in the art is deemed to be high.

The claims are broadly drawn to a humanized CC49 antibody, comprising: a light chain complementarity determining region (L-CDR)1, a L-CDR2, and a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, wherein a L-CDR3 of the humanized CC49 antibody or of any functional fragment of the humanized CC49 antibody comprises a non-conservative amino acid substitution at any position OR at any tyrosine residue of L-CDR3 OR substituting the tyrosine residue at position 91 with any amino acid, and wherein the humanized CC49 antibody has a high binding affinity for TAG-72, compared to a parent CC49 antibody, wherein L-CDR1 and L-CDR2 are any human L-CDR1 and L-CDR2 AND a humanized CC49 antibody, comprising: a variable light framework region and a variable heavy framework region of a human antibody; a light chain complementarity determining region (L-CDR)1, a L-CDR2, a L-CDR3, a heavy chain complementarity determining region (H-CDR)1, a H-CDR2, and a H-CDR3, wherein at least one complementarity determining region (CDR)

is a human antibody CDR and remaining CDRs are murine CC49 antibody CDRs; a non-conservative substitution of any residue is in the L-CDR3 of the antibody; and a substitution of any residue in any L-CDR or H-CDR of the antibody; wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody.

Thus, the claims broadly encompass a humanized CC49 antibody comprising any fragment of humanized CC49 antibody (as in lines 5-6 of claim 1); any non-conservative substitution of tyrosine to proline in L-CDR3 (as in claims 2 and 24); any non-conservative substitution at position 91 with any amino acid (as in claims 3 and 25); L-CDR1 and L-CDR2 are any human L-CDR1 and L-CDR2 (as in claim 6); any non-conservative substitution in L-CDR1 (as in claim 16); a variable light framework region and a variable heavy framework region (as in line 2 of claim 23); any two substitutions, wherein first substitution is in L-CDR3 and the second substitution is in any L-CDR of H-CDR (lines 8-11 of claim 23).

The specification discloses only two humanized CC49 antibody variants: (i) HuCC49V10-14 which consists of a non-conservative amino acid substitution at position 91, wherein the tyrosine at position 91 is substituted with proline and (ii) HuCC49V10-15 which consists of a non-conservative substitution of at position 91 in the L-CDR3 of the antibody, wherein the tyrosine at position 91 is substituted with proline, and a second substitution at position 27b of L-CDR1, wherein the valine at position 27b is substituted with leucine that exhibit high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody, HuCC49V10 (See Examples 1-5, in particular).

The specification discloses that the dissociation rates of only 6 isolated were lower than that of the parent antibody (HuCC49V10) as shown in Table 5 (Page 44, in particular) and the ELISA results show that the antigen-binding activity of only two variants, HuCC49V10-14 and HuCC49V10-15, was either comparable to or exceeded that of the parental HuCC49V10 (page 47, in particular). Further, in table 5, the relative affinity binding of CC49 antibodies show that only HuCC49V10-14 and HuCC49V10-15 exhibited a better/high binding activity compared to the parent HuCC49V10; and the Flow cytometric analysis, in figure 6, showed that only two variants, HuCC49V10-14 and HuCC49V10-15 show significantly better binding to the cells displaying TAG-72 on their surface (page 50, in particular). In addition, the studies in regard to the sera reactivity of HuCC49V10 variants indicated that only two variants, HuCC49V10-14 and HuCC49V10-15 showed not only significantly higher antigen binding affinity that that of HuCC49V10, but they also showed much lower reactivity to sera from patients who showed an anti-idiotypic response to the parental CC49 antibody (page 53, in particular).

The specification does not disclose any humanized CC49 antibody variants other than HuCC49V10-14 and HuCC49V10-15 which comprise any fragment of humanized CC49 antibody (as in lines 5-6 of claim 1); any non-conservative substitution of tyrosine to proline in L-CDR3 (as in claims 2 and 24); any non-conservative substitution at position 91 with any amino acid (as in claims 3 and 25); L-CDR1 and L-CDR2 are any human L-CDR1 and L-CDR2 (as in claim 6); any non-conservative substitution in L-CDR1 (as in claim 16); a variable light framework region and a variable heavy

framework region (as in line 2 of claim 23); any two substitutions, wherein first substitution is in L-CDR3 and the second substitution is in any L-CDR of H-CDR (lines 8-11 of claim 23) that have a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody, HuCC49V10. There are no working examples of humanized antibody variants other than HuCC49V10-14 and HuCC49V10-15 that have a high binding affinity for TAG-72 and are minimally immunogenic, compared to a parent CC49 antibody, HuCC49V10.

The state of the prior art is such that it is well established in the art that the formation of an intact antigen-binding site of antibodies routinely requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (Paul, Fundamental Immunology, 3rd Edition, 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). Even minor changes in the amino acid sequences of

the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79:1979-1983, March 1982). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Colman (Research in Immunology, 145:33-36, 1994) teaches that even a very conservative substitution may abolish binding or may have very little effect on the binding affinity (see pg. 35, top of left column and pg. 33, right column). It is unlikely that human antibodies comprising a variable region which does not contain all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their correct spatial orientation have the requisite RG1 binding function.

Although the specification discloses amino acid sequences deduced from the nucleotide sequences showed substitutions in LCDR3 of all the six variants, and such substitutions were limited to the positions 91, 93 and 94; whereas only one variant showed substitution in HCDR2, and two variants showed inadvertent mutation in position 27b of the LCDR1 (Page 45 and Table 2, in particular), the specification clearly discloses, in examples 1-5, that only two variants exhibited a high binding affinity for TAG-72 and are minimally immunogenic, compared to a parent CC49 antibody, HuCC49V10. The specification provides no direction or guidance regarding how to produce the myriad of humanized antibodies, which contain substitutions with the CDR(s) or which contain less than all four framework regions from both the light and heavy chain as broadly defined by the claims. Due to the unpredictability of art in

regard to the substitutions or deletions within the complementary determining regions, including the importance of the framework regions in maintaining the structural and functional integrity of an antibody, undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Additionally, Bendig M. M. (Methods: A Companion to Methods in Enzymology, 1995; 8:83-93) reviews that the general strategy for "humanizing" antibodies involves the substitution of all six CDRs from a rodent antibody that binds an antigen of interest, and that all six CDRs are involved in antigen binding (see entire document, but especially Figures 1-3). Similarly, the skilled artisan recognized a "chimeric" antibody to be an antibody in which both the heavy chain variable region (which comprises the three heavy chain CDRs) and the light chain variable region (which comprises the three light chain CDRs) of a rodent antibody are recombined with constant region sequences from a human antibody of a desired isotype (see entire document, but especially Figures 1-3). Thus, the state of the art recognized that it would be highly unpredictable that a humanized antibody comprising an antibody variable region but comprising less than all six CDRs of a parental antibody with a desired specificity would retain the antigen-binding function of the parental antibody. Thus, the minimal structure which the skilled artisan would consider predictive of the function of binding antigen or human CD28 includes six CDRs (three from the heavy chain variable region and three from the light chain variable region) from the same parental antibody in the context of framework

sequences which maintain their correct spatial orientation have the requisite antigen-binding function. While there are some publications, which acknowledge that CDR3 is important, the conformations of other CDRs as well as framework residues influence binding. MacCallum et al (J. Mol. Biol., 262, 732-745, 1996) analyzed many different antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right col.) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left col.). The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen binding site, is underscored by Casset et al (Biochemical and Biophysical Research Communications, 307:198-205, 2003), which constructed a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design and the peptide was designed with 27 residues formed by residues from 5 CDRs (see entire document). Casset et al also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left col.) and this is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (see page 202, left col.). It is unlikely that humanized antibodies, which do not contain all of the heavy and light chain CDRs of a parental antibody in their proper order and in the context of framework sequences which maintain their correct spatial orientation, have the requisite antigen binding function.

The specification provides insufficient evidence or nexus that would lead the skilled artisan to predict the ability of producing humanized antibody variants other than HuCC49V10-14 which consists of a non-conservative amino acid substitution at position 91, wherein the tyrosine at position 91 is substituted with proline; and HuCC49V10-15 which consists of a non-conservative substitution of at position 91 in the L-CDR3 of the antibody, wherein the tyrosine at position 91 is substituted with proline, and a second substitution at position 27b of L-CDR1, wherein the valine at position 27b is substituted with leucine that exhibit high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody, HuCC49V10 which comprise any fragment of humanized CC49 antibody; any non-conservative substitution of tyrosine to proline in L-CDR3; any non-conservative substitution at position 91 with any amino acid; L-CDR1 and L-CDR2 are any human L-CDR1 and L-CDR2; any non-conservative substitution in L-CDR1; a variable light framework region and a variable heavy framework region; any two substitutions, wherein first substitution is in L-CDR3 and the second substitution is in any L-CDR of H-CDR that have a high binding affinity for TAG-72 and is minimally immunogenic, compared to a parent CC49 antibody, HuCC49V10. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what

other species will work. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Paul W. E., Rudikoff et al, Coleman P. M. and Hanson et al, the lack of guidance and direction provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed humanized antibody variants that bind TAG-72 with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed humanized antibody variants and absent working examples providing evidence which is reasonably predictive that the claimed humanized antibody variants bind TAG-72, commensurate in scope with the claimed invention.

Conclusion

9. No claims are allowed

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone


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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
Ph: (571) 272-8789



DAVID J. BLANCHARD
PATENT EXAMINER